WHAT IS CLAIMED IS:

1. A compound comprising:

(1) a therapeutic agent capable of entering a target cell,

(2) an oligopeptide of the formula $(AA)_n$-AA^4-AA^3-AA^2-AA^1, wherein:

each AA independently represents an amino acid,

n is an integer from 0 to 16,

AA^4 represents a non-genetically-encoded amino acid,

AA^3 represents any amino acid,

AA^2 represents any amino acid, and

AA^1 represents any amino acid,

(3) a stabilizing group, and

(4) optionally, a linker group not cleavable by TOP,

wherein the oligopeptide is directly linked to the stabilizing group at a first attachment site of the oligopeptide and the oligopeptide is directly linked to the therapeutic agent or indirectly linked through the linker group to the therapeutic agent at a second attachment site of the oligopeptide,

wherein the stabilizing group hinders cleavage of the compound by enzymes present in whole blood, and

wherein the compound is cleavable by an enzyme associated with the target cell.

2. The compound of claim 1 wherein n is an integer from 0 to 8.

3. The compound of claim 1 wherein the target cell is a tumor or inflammatory cell.

4. A compound comprising:

(1) a therapeutic agent capable of entering a target cell,

(2) an oligopeptide of the formula $(AA)_n$-AA^4-AA^3-AA^2-AA^1, wherein:

each AA independently represents an amino acid,

n is an integer from 0 to 16,

AA^4 represents a non-genetically-encoded amino acid,

AA^3 represents any amino acid,

AA^2 represents any amino acid, and

AA^1 represents any amino acid,

(3) a stabilizing group, and

(4) optionally, a linker group not cleavable by TOP,

wherein the oligopeptide is directly linked to the stabilizing group at a first attachment site of the oligopeptide and the oligopeptide is directly linked to the therapeutic agent or indirectly linked through the linker group to the therapeutic agent at a second attachment site of the oligopeptide,

wherein the stabilizing group hinders cleavage of the compound by enzymes present in whole blood, and

wherein the compound is cleavable by a trouase.

5. A compound comprising:

(1) a therapeutic agent capable of entering a target cell,

(2) an oligopeptide of the formula $(AA)_n$-AA^4-AA^3-AA^2-AA^1, wherein:

each AA independently represents an amino acid,

n is an integer from 0 to 16,

AA^4 represents a non-genetically-encoded amino acid,

AA^3 represents any amino acid,

AA^2 represents any amino acid, and

AA^1 represents any amino acid,

(3) a stabilizing group, and

(4) optionally, a linker group not cleavable by TOP,

wherein the oligopeptide is directly linked to the stabilizing group at a first attachment site of the oligopeptide and the oligopeptide is directly linked to the therapeutic agent or indirectly linked through the linker group to the therapeutic agent at a second attachment site of the oligopeptide,

wherein the stabilizing group hinders cleavage of the compound by enzymes present in whole blood, and

wherein the compound is cleavable by TOP.

6. The compound of claim 5 wherein TOP is present in the extracellular vicinity of the target cell for the therapeutic agent.

7. The compound of claim 5 wherein TOP cleaves the linkage between AA^3 and AA^2 of the oligopeptide.

8. The compound of claim 5 being a prodrug having an active portion, wherein the active portion of the prodrug is more capable of entering the target cell after cleavage by TOP than prior to cleavage by TOP, the active portion including at least the therapeutic agent.

9. The compound of claim 8 wherein the active portion of the prodrug consists of the therapeutic agent.

10. The compound of claim 8 wherein the active portion of the prodrug includes the therapeutic agent and at least the linker group.

11. The compound of claim 8 wherein the active portion of the prodrug includes the therapeutic agent and AA^1 of the oligopeptide.

12. The compound of claim 11 wherein the active portion of the prodrug further comprises AA^2 of the oligopeptide linked to AA^1.

13. The compound of claim 5 wherein the oligopeptide is selected from the group consisting of: D-AlaThiβAlaβAlaLeuAlaLeu (SEQ ID NO: 1), ThiβAlaβAlaLeuAlaLeu (SEQ ID NO: 2), βAlaβAlaLeuAlaLeu (SEQ ID NO: 3), βAlaAlaAlaIle (SEQ ID NO: 4), βAlaAlaAlaLeu (SEQ ID NO: 5), βAlaPheTyrLeu (SEQ ID NO: 6), βAlaPheThrPhe (SEQ ID NO: 7), βAlaPheGlyIle (SEQ ID NO: 8), βAlaPheGlyLeu (SEQ ID NO: 9), βAlaPhePhePhe (SEQ ID NO: 10), βAlaPhePheIle (SEQ ID NO: 11), βAlaPhePheLeu (SEQ ID NO: 12), βAlaPheAlaIle (SEQ ID NO: 13), βAlaPheAlaLeu (SEQ ID NO: 14), ThiGlyAlaLeu (SEQ ID NO: 15), NalGlyAlaLeu (SEQ ID NO: 16), βAlaLeuTyrLeu

(SEQ ID NO: 17), βAlaLeuThiLeu (SEQ ID NO: 18), βAlaLeuThrPhe (SEQ ID NO: 19), βAlaLeuThrIle (SEQ ID NO: 20), βAlaLeuThrLeu (SEQ ID NO: 21), βAlaLeuSerLeu (SEQ ID NO: 22), βAlaLeuPyrLeu (SEQ ID NO: 23), βAlaLeuLeuLeu (SEQ ID NO: 24), βAlaLeuGlyPhe (SEQ ID NO: 25), βAlaLeuGlyIle (SEQ ID NO: 26), ThiLeuGlyLeu (SEQ ID NO: 27), βAlaLeuGlyLeu (SEQ ID NO: 28), AibLeuGlyLeu (SEQ ID NO: 29), βAlaLeuPheIle (SEQ ID NO: 30), βAlaLeuPheLeu (SEQ ID NO: 31), βAlaLeuAibLeu (SEQ ID NO: 32), βAlaLeuAlaAla (SEQ ID NO: 33), βAlaLeuAlaβAla (SEQ ID NO: 34), βAlaLeuAlaPhe (SEQ ID NO: 35), βAlaLeuAlaGly (SEQ ID NO: 36), βAlaLeuAlaIle (SEQ ID NO: 37), βAlaLeuAlaLeu (SEQ ID NO: 38), TicLeuAlaLeu (SEQ ID NO: 39), ThzLeuAlaLeu (SEQ ID NO: 40), ThiLeuAlaLeu (SEQ ID NO: 41), NalLeuAlaLeu (SEQ ID NO: 42), NAALeuAlaLeu (SEQ ID NO: 43), D-LeuLeuAlaLeu (SEQ ID NO: 44), D-AlaLeuAlaLeu (SEQ ID NO: 45), D-MetLeuAlaLeu (SEQ ID NO: 46), APPLeuAlaLeu (SEQ ID NO: 47), AmbLeuAlaLeu (SEQ ID NO: 48), βAlaLeuAlaNal (SEQ ID NO: 49), βAlaLeuAlaSer (SEQ ID NO: 50), βAlaLeuAlaTyr (SEQ ID NO: 51), βAlaMetTyrPhe (SEQ ID NO: 52), βAlaMetTyrLeu (SEQ ID NO: 53), βAlaMetGlyIle (SEQ ID NO: 54), ThiMetGlyLeu (SEQ ID NO: 55), βAlaMetPhePhe (SEQ ID NO: 56), βAlaMetPheIle (SEQ ID NO: 57), TicMetAlaLeu (SEQ ID NO: 58), NalMetAlaLeu (SEQ ID NO: 59), NAAMetAlaLeu (SEQ ID NO: 60), βAlaMetAlaLeu (SEQ ID NO: 61), APPMetAlaLeu (SEQ ID NO: 62), βAlaNleTyrIle (SEQ ID NO: 63), βAlaNleTyrLeu (SEQ ID NO: 64), βAlaNleThrIle (SEQ ID NO: 65), βAlaNleThrLeu (SEQ ID NO: 66), βAlaNleGlyPhe (SEQ ID NO: 67), βAlaNleGlyIle (SEQ ID NO: 68), βAlaNleGlyLeu (SEQ ID NO: 69), βAlaNlePheIle (SEQ ID NO: 70), βAlaNleAlaIle (SEQ ID NO: 71), βAlaNleAlaLeu (SEQ ID NO: 72), βAlaNleAlaPhe (SEQ ID NO: 73), βAlaNvaAlaLeu (SEQ ID NO: 74), βAlaPheTyrIle (SEQ ID NO: 75), ThiProGlyLeu (SEQ ID NO: 76), ThiProAlaLeu (SEQ ID NO: 77), NalProAlaLeu (SEQ ID NO: 78), βAlaProAlaLeu (SEQ ID NO: 79), βAlaPhe(Cl),AlaLeu (SEQ ID NO: 80), βAlaPhe(NO2),AlaIle (SEQ ID NO: 81), βAlaPhe(NO2),AlaLeu (SEQ ID NO: 82), βAlaPhgAlaLeu (SEQ ID NO: 83), βAlaPyrAlaLeu (SEQ ID NO: 84), TicThrGlyLeu (SEQ ID NO: 85), βAlaThiGlyIle (SEQ ID NO: 86), βAlaThiAlaLeu (SEQ ID NO: 87),

βAlaTicAlaIle (SEQ ID NO: 88), βAlaTicAlaLeu (SEQ ID NO: 89), βAlaValAlaLeu (SEQ ID NO: 90), βAlaTrpAlaLeu (SEQ ID NO: 91), βAlaTyrTyrPhe (SEQ ID NO: 92), βAlaTyrTyrIle (SEQ ID NO: 93), βAlaTyrTyrLeu (SEQ ID NO: 94), βAlaTyrThrLeu (SEQ ID NO: 95), βAlaTyrPheLeu (SEQ ID NO: 96), βAlaTyrGlyIle (SEQ ID NO: 97), ThiTyrGlyLeu (SEQ ID NO: 98), βAlaTyrGlyLeu (SEQ ID NO: 99), βAlaTyrPheIle (SEQ ID NO: 100), βAlaTyrAlaIle (SEQ ID NO: 101), ThiTyrAlaLeu (SEQ ID NO: 102), and βAlaTyrAlaLeu (SEQ ID NO: 103).

14. The compound of claim 5 wherein AA^1 of the oligopeptide is selected from the group consisting of Leucine, Phenylalanine, Isoleucine, Alanine, Glycine, Tyrosine, 2-Naphthylalanine, Serine, p-Cl-phenylalanine, p-Nitrophenylalanine, 1-Naphthylalanine, Threonine, Homoserine, Cyclohexylalanine, Thienylalanine, Homophenylalanine, Norleucine, and β-Alanine.

15. The compound of claim 5 wherein AA^2 of the oligopeptide is selected from the group consisting of Alanine, Leucine, Tyrosine, Glycine, Serine, 3-Pyridylalanine, 2-Thienylalanine, Norleucine, Homoserine, Homophenylalanine, p-Cl-phenylalanine, p-Nitrophenylalanine, Aminoisobutyric Acid, Threonine, and Phenylalanine.

16. The compound of claim 5 wherein AA^3 of the oligopeptide is selected from the group consisting of Leucine, Tyrosine, Phenylalanine, p-Cl-Phenylalanine, p-Nitrophenylalanine, Valine, Norleucine, Norvaline, Phenylglycine, Tryptophan, Tetrahydroisoquinoline-3-carboxylic acid, 3-Pyridylalanine, Alanine, Glycine, Thienylalanine, Methionine, Valine, and Proline.

17. The compound of claim 5 wherein AA^4 is selected from the group consisting of β-Alanine, Thiazolidine-4-carboxylic acid, 2-Thienylalanine, 2-Naphthylalanine, D-Alanine, D-Leucine, D-Methionine, D-Phenylalanine, 3-Amino-3-phenylpropionic acid, γ-Aminobutyric acid, 3-Amino-4,4-diphenylbutyric acid, Tetrahydroisoquinoline-3-carboxylic acid, 4-Aminomethylbenzoic acid, and Aminoisobutyric acid.

18. The compound of claim 5 wherein the stabilizing group is a dicarboxylic or higher order carboxylic acid.

19. The compound of claim 5 wherein the stabilizing group is selected from the group consisting of : succinic acid, adipic acid, glutaric acid, phthalic acid, diglycolic acid, fumaric acid, naphthalene dicarboxylic acid, pyroglutamic acid, acetic acid, 1-naphthylcarboxylic acid, 2-naphthylcarboxylic acid, 1,8-naphthyl dicarboxylic acid, aconitic acid, carboxycinnamic acid, triazole dicarboxylic acid, gluconic acid, 4-carboxyphenyl boronic acid, polyethylene glycolic acid, butane disulfonic acid, and maleic acid.

20. The compound of claim 5 wherein the stabilizing group is a non-genetically encoded amino acid having four or more carbons.

21. The compound of claim 5 wherein the stabilizing group is one of aspartic acid linked to the oligopeptide at the β-carboxy group of the aspartic acid or glutamic acid linked to the oligopeptide at the γ-carboxy group of the glutamic acid.

22. The compound of claim 5 wherein the stabilizing group is negatively charged or neutral.

23. The compound of claim 5 wherein the stabilizing group is selected to reduce interaction between the compound and endothelial cells that line blood vessels when administered intravenously to the patient.

24. The compound of claim 5 wherein the therapeutic agent is selected from the group consisting of Alkylating Agents, Antiproliferative agents, Tubulin Binding agents, Vinca Alkaloids, Enediynes, Podophyllotoxins or Podophyllotoxin derivatives, the Pteridine family of drugs, Taxanes, Anthracyclines, Dolastatins, Topoiosomerase inhibitors, and Platinum complex chemotherapeutic agents.

25. The compound of claim 5 wherein the therapeutic agent is selected from the group consisting of Doxorubicin, Daunorubicin, Vinblastine, Vincristine, Calicheamicin, Etoposide, Etoposide phosphate, CC-1065, Duocarmycin, KW-2189, Methotrexate, Methopterin, Aminopterin, Dichloromethotrexate, Docetaxel, Paclitaxel, Epithiolone, Combretastatin, Combretastatin A4 Phosphate, Dolastatin 10, Dolastatin 11, Dolastatin 15, Topotecan, Camptothecin, Mitomycin C, Porfiromycin, 5-Fluorouracil, 6-Mercaptopurine, Fludarabine, Tamoxifen, Cytosine arabinoside, Adenosine arabinoside, Colchicine, Cisplatin, Carboplatin, Mitomycin C, Bleomycin, Melphalan, Chloroquine, Cyclosporin A, a derivative of any of the foregoing, and an analog of any of the foregoing.

26. The compound of claim 5 wherein the oligopeptide is directly linked to the therapeutic agent.

27. The compound of claim 5 wherein the oligopeptide sequence is indirectly linked to the therapeutic agent at the second attachment site of the oligopeptide via a linker group, the linker group selected from the group consisting of amino caproic acid, a hydrazide group, an ester group, an ether group, and a sulphydryl group.

28. The compound of claim 5 wherein the compound is selected from the group consisting of Suc-βAla-Leu-Ala-Leu-Dox, Suc-βAla-Leu-Ala-Leu-Dnr, and Glutaryl-βAla-Leu-Ala-Leu-Dox.

29. The compound of claim 5 wherein the compound is resistant to cleavage by CD10.

30. A conjugate comprising an oligopeptide of the formula $(AA)_n$-AA^4-AA^3-AA^2-AA^1, wherein:

each AA independently represents an amino acid,

n is an integer from 0 to 16,

AA^4 represents a non-genetically-encoded amino acid,

AA^3 represents any amino acid,

AA^2 represents any amino acid, and

AA^1 represents any amino acid,

wherein the oligopeptide is cleavable by TOP.

31. The conjugate of claim 30 wherein the oligopeptide is linked to a stabilizing group.

32. The conjugate of claim 30 wherein the oligopeptide is linked to a therapeutic agent.

33. An oligopeptide selected from the group consisting of D-AlaThiβAlaβAlaLeuAlaLeu (SEQ ID NO: 1), ThiβAlaβAlaLeuAlaLeu (SEQ ID NO: 2), βAlaβAlaLeuAlaLeu (SEQ ID NO: 3), βAlaAlaAlaIle (SEQ ID NO: 4), βAlaAlaAlaLeu (SEQ ID NO: 5), βAlaPheTyrLeu (SEQ ID NO: 6), βAlaPheThrPhe (SEQ ID NO: 7), βAlaPheGlyIle (SEQ ID NO: 8), βAlaPheGlyLeu (SEQ ID NO: 9), βAlaPhePhePhe (SEQ ID NO: 10), βAlaPhePheIle (SEQ ID NO: 11), βAlaPhePheLeu (SEQ ID NO: 12), βAlaPheAlaIle (SEQ ID NO: 13), βAlaPheAlaLeu (SEQ ID NO: 14), ThiGlyAlaLeu (SEQ ID NO: 15), NalGlyAlaLeu (SEQ ID NO: 16), βAlaLeuTyrLeu (SEQ ID NO: 17), βAlaLeuThiLeu (SEQ ID NO: 18), βAlaLeuThrPhe (SEQ ID NO: 19), βAlaLeuThrIle (SEQ ID NO: 20), βAlaLeuThrLeu (SEQ ID NO: 21), βAlaLeuSerLeu (SEQ ID NO: 22), βAlaLeuPyrLeu (SEQ ID NO: 23), βAlaLeuLeuLeu (SEQ ID NO: 24), βAlaLeuGlyPhe (SEQ ID NO: 25), βAlaLeuGlyIle (SEQ ID NO: 26), ThiLeuGlyLeu (SEQ ID NO: 27), βAlaLeuGlyLeu (SEQ ID NO: 28), AibLeuGlyLeu (SEQ ID NO: 29), βAlaLeuPheIle (SEQ ID NO: 30), βAlaLeuPheLeu (SEQ ID NO: 31), βAlaLeuAibLeu (SEQ ID NO: 32), βAlaLeuAlaAla (SEQ ID NO: 33), βAlaLeuAlaβAla (SEQ ID NO: 34), βAlaLeuAlaPhe (SEQ ID NO: 35), βAlaLeuAlaGly (SEQ ID NO: 36), βAlaLeuAlaIle (SEQ ID NO: 37), βAlaLeuAlaLeu (SEQ ID NO: 38), TicLeuAlaLeu (SEQ ID NO: 39), ThzLeuAlaLeu (SEQ ID NO: 40), ThiLeuAlaLeu (SEQ ID NO: 41), NalLeuAlaLeu (SEQ ID NO: 42), NAALeuAlaLeu (SEQ ID NO: 43), D-LeuLeuAlaLeu (SEQ ID NO:

44), D-AlaLeuAlaLeu (SEQ ID NO: 45), D-MetLeuAlaLeu (SEQ ID NO: 46), APPLeuAlaLeu (SEQ ID NO: 47), AmbLeuAlaLeu (SEQ ID NO: 48), βAlaLeuAlaNal (SEQ ID NO: 49), βAlaLeuAlaSer (SEQ ID NO: 50), βAlaLeuAlaTyr (SEQ ID NO: 51), βAlaMetTyrPhe (SEQ ID NO: 52), βAlaMetTyrLeu (SEQ ID NO: 53), βAlaMetGlyIle (SEQ ID NO: 54), ThiMetGlyLeu (SEQ ID NO: 55), βAlaMetPhePhe (SEQ ID NO: 56), βAlaMetPheIle (SEQ ID NO: 57), TicMetAlaLeu (SEQ ID NO: 58), NalMetAlaLeu (SEQ ID NO: 59), NAAMetAlaLeu (SEQ ID NO: 60), βAlaMetAlaLeu (SEQ ID NO: 61), APPMetAlaLeu (SEQ ID NO: 62), βAlaNleTyrIle (SEQ ID NO: 63), βAlaNleTyrLeu (SEQ ID NO: 64), βAlaNleThrIle (SEQ ID NO: 65), βAlaNleThrLeu (SEQ ID NO: 66), βAlaNleGlyPhe (SEQ ID NO: 67), βAlaNleGlyIle (SEQ ID NO: 68), βAlaNleGlyLeu (SEQ ID NO: 69), βAlaNlePheIle (SEQ ID NO: 70), βAlaNleAlaIle (SEQ ID NO: 71), βAlaNleAlaLeu (SEQ ID NO: 72), βAlaNleAlaPhe (SEQ ID NO: 73), βAlaNvaAlaLeu (SEQ ID NO: 74), βAlaPheTyrIle (SEQ ID NO: 75), ThiProGlyLeu (SEQ ID NO: 76), ThiProAlaLeu (SEQ ID NO: 77), NalProAlaLeu (SEQ ID NO: 78), βAlaProAlaLeu (SEQ ID NO: 79), βAlaPhe(Cl),AlaLeu (SEQ ID NO: 80), βAlaPhe(NO2),AlaIle (SEQ ID NO: 81), βAlaPhe(NO2),AlaLeu (SEQ ID NO: 82), βAlaPhgAlaLeu (SEQ ID NO: 83), βAlaPyrAlaLeu (SEQ ID NO: 84), TicThrGlyLeu (SEQ ID NO: 85), βAlaThiGlyIle (SEQ ID NO: 86), βAlaThiAlaLeu (SEQ ID NO: 87), βAlaTicAlaIle (SEQ ID NO: 88), βAlaTicAlaLeu (SEQ ID NO: 89), βAlaValAlaLeu (SEQ ID NO: 90), βAlaTrpAlaLeu (SEQ ID NO: 91), βAlaTyrTyrPhe (SEQ ID NO: 92), βAlaTyrTyrIle (SEQ ID NO: 93), βAlaTyrTyrLeu (SEQ ID NO: 94), βAlaTyrThrLeu (SEQ ID NO: 95), βAlaTyrPheLeu (SEQ ID NO: 96), βAlaTyrGlyIle (SEQ ID NO: 97), ThiTyrGlyLeu (SEQ ID NO: 98), βAlaTyrGlyLeu (SEQ ID NO: 99), βAlaTyrPheIle (SEQ ID NO: 100), βAlaTyrAlaIle (SEQ ID NO: 101), ThiTyrAlaLeu (SEQ ID NO: 102), and βAlaTyrAlaLeu (SEQ ID NO: 103).

34. A conjugate comprising an oligopeptide selected from the group consisting of D-AlaThiβAlaβAlaLeuAlaLeu (SEQ ID NO: 1), ThiβAlaβAlaLeuAlaLeu (SEQ ID NO: 2), βAlaβAlaLeuAlaLeu (SEQ ID NO: 3), βAlaAlaAlaIle (SEQ ID NO: 4), βAlaAlaAlaLeu

(SEQ ID NO: 5), βAlaPheTyrLeu (SEQ ID NO: 6), βAlaPheThrPhe (SEQ ID NO: 7), βAlaPheGlyIle (SEQ ID NO: 8), βAlaPheGlyLeu (SEQ ID NO: 9), βAlaPhePhePhe (SEQ ID NO: 10), βAlaPhePheIle (SEQ ID NO: 11), βAlaPhePheLeu (SEQ ID NO: 12), βAlaPheAlaIle (SEQ ID NO: 13), βAlaPheAlaLeu (SEQ ID NO: 14), ThiGlyAlaLeu (SEQ ID NO: 15), NalGlyAlaLeu (SEQ ID NO: 16), βAlaLeuTyrLeu (SEQ ID NO: 17), βAlaLeuThiLeu (SEQ ID NO: 18), βAlaLeuThrPhe (SEQ ID NO: 19), βAlaLeuThrIle (SEQ ID NO: 20), βAlaLeuThrLeu (SEQ ID NO: 21), βAlaLeuSerLeu (SEQ ID NO: 22), βAlaLeuPyrLeu (SEQ ID NO: 23), βAlaLeuLeuLeu (SEQ ID NO: 24), βAlaLeuGlyPhe (SEQ ID NO: 25), βAlaLeuGlyIle (SEQ ID NO: 26), ThiLeuGlyLeu (SEQ ID NO: 27), βAlaLeuGlyLeu (SEQ ID NO: 28), AibLeuGlyLeu (SEQ ID NO: 29), βAlaLeuPheIle (SEQ ID NO: 30), βAlaLeuPheLeu (SEQ ID NO: 31), βAlaLeuAibLeu (SEQ ID NO: 32), βAlaLeuAlaAla (SEQ ID NO: 33), βAlaLeuAlaβAla (SEQ ID NO: 34), βAlaLeuAlaPhe (SEQ ID NO: 35), βAlaLeuAlaGly (SEQ ID NO: 36), βAlaLeuAlaIle (SEQ ID NO: 37), βAlaLeuAlaLeu (SEQ ID NO: 38), TicLeuAlaLeu (SEQ ID NO: 39), ThzLeuAlaLeu (SEQ ID NO: 40), ThiLeuAlaLeu (SEQ ID NO: 41), NalLeuAlaLeu (SEQ ID NO: 42), NAALeuAlaLeu (SEQ ID NO: 43), D-LeuLeuAlaLeu (SEQ ID NO: 44), D-AlaLeuAlaLeu (SEQ ID NO: 45), D-MetLeuAlaLeu (SEQ ID NO: 46), APPLeuAlaLeu (SEQ ID NO: 47), AmbLeuAlaLeu (SEQ ID NO: 48), βAlaLeuAlaNal (SEQ ID NO: 49), βAlaLeuAlaSer (SEQ ID NO: 50), βAlaLeuAlaTyr (SEQ ID NO: 51), βAlaMetTyrPhe (SEQ ID NO: 52), βAlaMetTyrLeu (SEQ ID NO: 53), βAlaMetGlyIle (SEQ ID NO: 54), ThiMetGlyLeu (SEQ ID NO: 55), βAlaMetPhePhe (SEQ ID NO: 56), βAlaMetPheIle (SEQ ID NO: 57), TicMetAlaLeu (SEQ ID NO: 58), NalMetAlaLeu (SEQ ID NO: 59), NAAMetAlaLeu (SEQ ID NO: 60), βAlaMetAlaLeu (SEQ ID NO: 61), APPMetAlaLeu (SEQ ID NO: 62), βAlaNleTyrIle (SEQ ID NO: 63), βAlaNleTyrLeu (SEQ ID NO: 64), βAlaNleThrIle (SEQ ID NO: 65), βAlaNleThrLeu (SEQ ID NO: 66), βAlaNleGlyPhe (SEQ ID NO: 67), βAlaNleGlyIle (SEQ ID NO: 68), βAlaNleGlyLeu (SEQ ID NO: 69), βAlaNlePheIle (SEQ ID NO: 70), βAlaNleAlaIle (SEQ ID NO: 71), βAlaNleAlaLeu (SEQ ID NO: 72), βAlaNleAlaPhe (SEQ ID NO: 73), βAlaNvaAlaLeu (SEQ ID NO: 74), βAlaPheTyrIle (SEQ ID NO: 75), ThiProGlyLeu

(SEQ ID NO: 76), ThiProAlaLeu (SEQ ID NO: 77), NalProAlaLeu (SEQ ID NO: 78), βAlaProAlaLeu (SEQ ID NO: 79), βAlaPhe(Cl),AlaLeu (SEQ ID NO: 80), βAlaPhe(NO2),AlaIle (SEQ ID NO: 81), βAlaPhe(NO2),AlaLeu (SEQ ID NO: 82), βAlaPhgAlaLeu (SEQ ID NO: 83), βAlaPyrAlaLeu (SEQ ID NO: 84), TicThrGlyLeu (SEQ ID NO: 85), βAlaThiGlyIle (SEQ ID NO: 86), βAlaThiAlaLeu (SEQ ID NO: 87), βAlaTicAlaIle (SEQ ID NO: 88), βAlaTicAlaLeu (SEQ ID NO: 89), βAlaValAlaLeu (SEQ ID NO: 90), βAlaTrpAlaLeu (SEQ ID NO: 91), βAlaTyrTyrPhe (SEQ ID NO: 92), βAlaTyrTyrIle (SEQ ID NO: 93), βAlaTyrTyrLeu (SEQ ID NO: 94), βAlaTyrThrLeu (SEQ ID NO: 95), βAlaTyrPheLeu (SEQ ID NO: 96), βAlaTyrGlyIle (SEQ ID NO: 97), ThiTyrGlyLeu (SEQ ID NO: 98), βAlaTyrGlyLeu (SEQ ID NO: 99), βAlaTyrPheIle (SEQ ID NO: 100), βAlaTyrAlaIle (SEQ ID NO: 101), ThiTyrAlaLeu (SEQ ID NO: 102), and βAlaTyrAlaLeu (SEQ ID NO: 103).

35. The conjugate of claim 34 wherein the oligopeptide is linked to a stabilizing group or a therapeutic agent or both.

36. A conjugate comprising the oligopeptide βAla-Leu-Ala-Leu (SEQ ID NO: 38) linked to a stabilizing group or a therapeutic agent or both.

37. A pharmaceutical composition comprising

(1) a compound comprising:

(a) a therapeutic agent capable of entering a target cell,

(b) an oligopeptide of the formula $(AA)_n$-AA^4-AA^3-AA^2-AA^1,

wherein:

each AA independently represents an amino acid,

n is an integer from 0 to 16,

AA^4 represents a non-genetically-encoded amino acid,

AA^3 represents any amino acid,

AA^2 represents any amino acid, and

AA^1 represents any amino acid,

(c) a stabilizing group, and

(d) optionally, a linker group not cleavable by TOP,

wherein the oligopeptide is directly linked to the stabilizing group at a first attachment site of the oligopeptide and the oligopeptide is directly linked to the therapeutic agent or indirectly linked through the linker group to the therapeutic agent at a second attachment site of the oligopeptide,

wherein the stabilizing group hinders cleavage of the compound by enzymes present in whole blood, and

wherein the compound is cleavable by an enzyme associated with the target cell, and

(2) a pharmaceutically acceptable carrier.

38. The pharmaceutical composition of claim 37 wherein the enzyme associated with the target cell is TOP.

39. A method for treating a patient, the method comprising:
administering to the patient a therapeutically effective amount of a compound comprising:

(1) a therapeutic agent capable of entering a target cell,

(2) an oligopeptide of the formula $(AA)_n$-AA^4-AA^3-AA^2-AA^1, wherein:

each AA independently represents an amino acid,

n is an integer from 0 to 16,

AA^4 represents a non-genetically-encoded amino acid,

AA^3 represents any amino acid,

AA^2 represents any amino acid, and

AA^1 represents any amino acid,

(3) a stabilizing group, and

(4) optionally, a linker group not cleavable by TOP,

wherein the oligopeptide is directly linked to the stabilizing group at a first attachment site of the oligopeptide and the oligopeptide is directly linked to the therapeutic agent or indirectly linked through the linker group to the therapeutic agent at a second attachment site of the oligopeptide,

wherein the stabilizing group hinders cleavage of the compound by enzymes present in whole blood, and

wherein the compound is cleavable by an enzyme associated with the target cell.

40. The method of claim 39 wherein the enzyme associated with the target cell is a trouase.

41. The method of claim 39 wherein the trouase is TOP.

42. The method of claim 39 wherein the compound is administered intravenously.

43. The method of claim 39 wherein the patient is treated for a medical condition selected from the group consisting of cancer, neoplastic diseases, tumors, inflammatory diseases, and infectious diseases.

44. The method of claim 39 wherein the target cell is multi-drug resistant.

45. A method of designing a prodrug for administration to a patient, the method comprising:

(1) identifying an oligopeptide of the formula $(AA)_n$-AA^4-AA^3-AA^2-AA^1, wherein:

each AA independently represents an amino acid,

n is an integer from 0 to 16,

AA^4 represents a non-genetically-encoded amino acid,

AA^3 represents any amino acid,

AA^2 represents any amino acid, and

AA^1 represents any amino acid,

(2) linking the oligopeptide at a first attachment site of the oligopeptide to a stabilizing group that hinders cleavage of the oligopeptide by enzymes present in whole blood, and

(3) directly or indirectly linking the oligopeptide to a therapeutic agent at a second attachment site of the oligopeptide,

wherein steps (2) and (3) may be performed in any order or concurrently and further wherein a conjugate is formed by performance of steps (1) through (3),

(4) testing if the conjugate is cleavable by TOP, and

(5) selecting the conjugate as a prodrug if the conjugate is cleavable by TOP.

46. The method of claim 45 wherein the first attachment site is the N-terminus of the oligopeptide.

47. The method of claim 45 wherein the second attachment site is the C-terminus of the oligopeptide.

48. The method of claim 45 wherein the first attachment site is the C-terminus of the oligopeptide.

49. The method of claim 45 wherein the second attachment site is the N-terminus of the oligopeptide.

50. A prodrug designed by the method of claim 45.

51. A method of treating resistance to a therapeutic agent in a patient in need of such treatment, the method comprising:

administering to the patient a therapeutically effective amount of a compound comprising:

(1) a therapeutic agent capable of entering a target cell,

(2) an oligopeptide of the formula $(AA)_n$-AA^4-AA^3-AA^2-AA^1, wherein:

each AA independently represents an amino acid,

n is an integer from 0 to 16,

AA^4 represents a non-genetically-encoded amino acid,

AA^3 represents any amino acid,

AA^2 represents any amino acid, and

AA^1 represents any amino acid,

(3) a stabilizing group, and

(4) optionally, a linker group not cleavable by TOP,

wherein the oligopeptide is directly linked to the stabilizing group at a first attachment site of the oligopeptide and the oligopeptide is directly linked to the therapeutic agent or indirectly linked through the linker group to the therapeutic agent at a second attachment site of the oligopeptide,

wherein the stabilizing group hinders cleavage of the compound by enzymes present in whole blood, and

wherein the compound is cleavable by TOP.

52. A method for decreasing toxicity of a therapeutic agent wherein the therapeutic agent is intended for administration to a patient, the method comprising:

covalently forming a prodrug by linking an oligopeptide cleavable by TOP to a stabilizing group at a first attachment site of the oligopeptide and directly or indirectly linking the therapeutic agent at a second attachment site of the oligopeptide, the prodrug being cleavable by TOP, whereby the prodrug provides for decreased toxicity of the therapeutic agent when administered to the patient.

53. The method of claim 52 wherein the prodrug allows for administration of an increased dosage of the therapeutic agent in prodrug form to the patient relative to the dosage of the therapeutic agent in unconjugated form.

54. The method of claim 52 wherein the oligopeptide is of the formula $(AA)_n$-AA^4-AA^3-AA^2-AA^1, wherein:

each AA independently represents an amino acid,

n is an integer from 0 to 16,

AA^4 represents a non-genetically-encoded amino acid,

AA^3 represents any amino acid,

AA^2 represents any amino acid, and

AA^1 represents any amino acid.

55. An article of manufacture for diagnosis or assay comprising:

(1) a compound comprising:

(a) a marker,

(b) an oligopeptide of the formula $(AA)_n$-AA^4-AA^3-AA^2-AA^1,

wherein:

each AA independently represents an amino acid,

n is an integer from 0 to 16,

AA^4 represents a non-genetically-encoded amino acid,

AA^3 represents any amino acid,

AA^2 represents any amino acid, and

AA^1 represents any amino acid,

(c) a stabilizing group, and

(d) optionally, a linker group not cleavable by TOP,

wherein the oligopeptide is directly linked to the stabilizing group at a first attachment site of the oligopeptide and the oligopeptide is directly linked to the marker or indirectly linked through the linker group to the marker at a second attachment site of the oligopeptide,

wherein the stabilizing group hinders cleavage of the compound by enzymes present in whole blood, and

wherein the compound is cleavable by TOP, and

(2) optionally at least one reagent useful in the detection of said marker.

56. In a method of making a prodrug, a method of removing free therapeutic agent comprising:

(1) coupling an optionally protected stabilizing group-oligopeptide conjugate with the free therapeutic agent,

(2) contacting the reactants of step (1) with a polymeric resin to bind free therapeutic agent remaining after step (1) to form a therapeutic agent-polymeric resin complex, and

(3) removing the therapeutic agent-polymeric resin complex.

57. The method of claim 56 wherein the polymeric resin is selected from the group consisting of polystyrene isocyanate, polystyrene methylisocyanate, polystyrene thioisocyanate, polystyrene methylthioisocyanate, polystyrene sulfonyl chloride, polystyrene methylsulfonyl chloride, and polystyrene benzaldehyde.

58. The method of claim 56 wherein the optionally protected stabilizing group-oligopeptide conjugate includes an oligopeptide of the formula $(AA)_n$-AA^4-AA^3-AA^2-AA^1, wherein:

each AA independently represents an amino acid,

n is an integer from 0 to 16,

AA^4 represents a non-genetically-encoded amino acid,

AA^3 represents any amino acid,

AA^2 represents any amino acid, and

AA^1 represents any amino acid.

59. A method of making a prodrug compound agent comprising the following steps:

(1) activating an Fmoc-protected oligopeptide with an activating agent in the presence of a therapeutic agent to make a Fmoc-protected oligopeptide therapeutic agent conjugate,

(2) deprotecting the Fmoc-protected oligopeptide therapeutic agent by contacting it with a base,

(3) reacting the oligopeptide therapeutic agent with a stabilizing group,

(4) neutralizing the stabilizing group-oligopeptide therapeutic agent conjugate with a pharmaceutically acceptable salt.

60. The method of claim 59, wherein the oligopeptide is the Fmoc-form of β-AlaLeuAlaLeu.

61. The method of claim 59, wherein the therapeutic agent is an anthracycline.

62. The method of claim 59, wherein the step of activating an Fmoc-protected oligopeptide with an activating agent further comprises selecting an activating agent from the group consisting of HATU, HBTU, DCC, DIC, DCC+HOBt, EDC, OSu, and PyBOP.

63. The method of claim 62, wherein the step of activating an Fmoc-protected oligopeptide includes using HATU or HBTU activating agent.

64. The method of claim 59, wherein the step of deprotecting the Fmoc-protected oligopeptide therapeutic agent further comprises selecting from the group consisting of piperidine, DBU, DBN, DBO, triethylamine, and NaOH.

65. The method of claim 59, wherein the step of reacting the oligopeptide therapeutic agent with a stabilizing group uses an anhydride or an activated ester of the stabilizing group.

66. A composition made by the method of claim 59.

67. A method of making a prodrug compound comprising the following steps:

(1) activating an alkyl or allyl ester-protected-stabilizing group oligopeptide with an activating agent in the presence of a therapeutic agent to make an alkyl- or allyl-ester-protected stabilizing group oligopeptide therapeutic agent conjugate,

(2) deprotecting the alkyl or allyl ester-protected-stabilizing group oligopeptide therapeutic agent, and

(3) neutralizing the stabilizing group-oligopeptide therapeutic agent with a pharmaceutically acceptable salt.

68. The method of claim 67, wherein the alkyl or allyl ester-protected stabilizing group oligopeptide is protected by a methyl or ethyl ester group.

69. The method of claim 67, wherein the alkyl or allyl ester-protected stabilizing group oligopeptide is methylsuccinyl protected β-AlaLeuAlaLeu.

70. The method of claim 67, wherein the therapeutic agent is an anthracycline.

71. The method of claim 67, wherein the step of activating the alkyl or allyl ester-protected stabilizing group oligopeptide with an activating agent comprises selecting from the group consisting of HATU, HBTU, DCC, DIC, DCC+HOBt, EDC, OSu, and PyBOP.

72. The method of claim 67, wherein the step of deprotecting the alkyl or allyl ester-protected stabilizing group oligopeptide therapeutic agent conjugate further comprises deprotecting with an enzyme selected from the group consisting of an esterase, pig liver esterase, *Candida antartica* B lipase, *Candida rugosa* lipase, *Pseudomonas cepacia* lipase, CLEC-CAB (crosslinked *Candida antartica* B lipase), CLEC-CR (crosslinked *Candida rugosa* lipase), CLEC-PC (*Pseudomonas cepacia* lipase) and Chirazyme (esterase immobilized on sepharose), CHIRO CLEC-PC™, and Sepharose-immobilized *Candida Antarctica* B lipase.

73. The method of claim 67, wherein the concentration of the alkyl or allyl ester-protected stabilizing group oligopeptide therapeutic agent is 1-25 % in the conjugation solvent and the deprotection solvent.

74. The method of claim 67, wherein the alkyl or allyl ester-protected stabilizing group is alkyl hemisuccinyl ester.

75. The method of claim 67, wherein the step of deprotecting the alkyl or allyl ester-protected stabilizing group oligopeptide therapeutic agent further comprises deprotecting with $Pd(P(Ph_3)_4)$.

76. A composition made by the method of claim 67.

77. A method of making a prodrug compound comprising the following steps:

(1) coupling an alkyl or allyl ester protected stabilizing group oligopeptide and a therapeutic agent in the presence of an activating agent to make an alkyl or allyl ester protected stabilizing group-oligopeptide-therapeutic agent conjugate,

(2) removing uncoupled therapeutic agent that remains after the coupling step, and

(3) deprotecting the alkyl or allyl ester protected stabilizing group oligopeptide therapeutic agent conjugate to make the stabilizing group-oligopeptide-therapeutic agent prodrug compound.

78. The method of claim 77 wherein the alkyl or allyl ester protected stabilizing group-oligopeptide and the therapeutic agent are present in a molar ratio of between 2:1 and 1:1, inclusive.

79. The method of claim 78 wherein the molar ratio is between 1.75:1 and 1.5:1, inclusive.

80. The method of claim 79 wherein the molar ratio is 1.66:1.

81. The method of claim 77 wherein the coupling step comprises:

(a) combining the alkyl or allyl ester protected stabilizing group oligopeptide and the therapeutic agent in DMF,

(b) adding DIEA,

(c) reacting the alkyl or allyl ester protected stabilizing group oligopeptide and the therapeutic agent in the presence of the activating agent to form the conjugate, and

(d) precipitating the conjugate by adding a brine solution to form a precipitate.

82. The method of claim 77 wherein the therapeutic agent is an anthracycline.

83. The method of claim 82 wherein the anthracycline is doxorubicin.

84. The method of claim 81 wherein the activating agent is HATU.

85. The method of claim 81 wherein the DIEA and the alkyl or allyl ester protected stabilizing group-oligopeptide are present in a molar ratio between 3:1 and 1.5:1.

86. The method of claim 85 wherein the molar ratio is between 2.5:1 and 2:1.

87. The method of claim 86 wherein the molar ratio is 2.18:1.

88. The method of claim 81 wherein the reacting step is performed at 0°C.

89. The method of claim 81 wherein the reacting step is performed for 30 minutes.

90. The method of claim 84 wherein the activating agent and the alkyl or allyl ester protected stabilizing group-oligopeptide are present in a molar ratio between 1.5:1 and 1:1.

91. The method of claim 90 wherein the molar ratio is 1.1:1.

92. The method of claim 81 wherein the brine solution is between 20% (w/v) and 40% (w/v) NaCl in water.

93. The method of claim 92 wherein the brine solution is between 25% (w/v) and 35% (w/v) NaCl in water.

94. The method of claim 93 wherein the brine solution is 30% (w/v) NaCl in water.

95. The method of claim 81 wherein the precipitating step is performed at a pH between 5.0 and 7.0, inclusive.

96. The method of claim 95 wherein the pH is between 5.8 and 6.0, inclusive.

97. The method of claim 77 wherein the removing step comprises:

(a) dissolving the conjugate in DMF,

(b) dissolving a scavenger resin in anhydrous DMF,

(c) adding the alkyl or allyl ester protected stabilizing group oligopeptide therapeutic agent conjugate formed in the coupling step to the scavenger resin to form a conjugate-resin mixture,

(d) maintaining the mixture at between 0°C and 30°C for 2 to 24 hours wherein the uncoupled therapeutic agent reacts with the resin,

(e) removing the resin from the mixture, and

(f) precipitating the remainder by adding a brine solution to form a precipitate of the alkyl or allyl ester protected stabilizing group oligopeptide therapeutic agent conjugate.

98. The method of claim 97 wherein the scavenger resin is selected from the group consisting of polystyrene isocyanate, polystyrene methylisocyanate, polystyrene thioisocyanate, polystyrene methylthioisocyanate, polystyrene sulfonyl chloride, polystyrene methylsulfonyl chloride, and polystyrene benzaldehyde.

99. The method of claim 98 wherein the scavenger resin is polystyrene isocyanate.

100. The method of claim 77 wherein the deprotecting step further comprises deprotecting with an enzyme.

101. The method of claim 100 wherein the enzyme is an esterase.

102. The method of claim 101 wherein the esterase is selected from the group consisting of pig liver esterase, *Candida antartica* B lipase, *Candida rugosa* lipase, *Pseudomonas cepacia* lipase, CLEC-CAB (crosslinked *Candida antartica* B lipase), CLEC-CR (crosslinked *Candida rugosa* lipase), CLEC-PC (*Pseudomonas cepacia* lipase) and Chirazyme (esterase immobilized on sepharose).

103. The method of claim 102 wherein the esterase is *Candida Antarctica* B lipase.

104. The method of claim 101 wherein the esterase is cross-linked or immobilized on a solid support.

105. The method of claim 104 wherein the deprotecting step comprises:

(a) washing the enzyme to remove free enzyme,

(b) adding the washed enzyme to the alkyl or allyl ester protected stabilizing group-oligopeptide-therapeutic agent conjugate,

(c) reacting the enzyme with the conjugate at between 15°C and 40°C, inclusive, at a pH between 5.0 and 8.0, inclusive, for at least 18 hours, to create the stabilizing group-oligopeptide-therapeutic agent prodrug compound, and

(d) separating the enzyme from the prodrug compound.

106. The method of claim 105, further comprising adding additional enzyme after the step of reacting the enzyme with the conjugate, wherein the additional enzyme is crosslinked or immobilized on a solid support.

107. A method of making a prodrug compound comprising the following steps:

(1) activating a trityl-protected oligopeptide with an activating agent in the presence of a therapeutic agent to make a trityl-protected oligopeptide therapeutic agent conjugate,

(2) deprotecting the trityl-protected oligopeptide therapeutic agent conjugate under acidic conditions for 30-120 minutes at 0 to 25 °C,

(3) reacting the oligopeptide-therapeutic agent with a stabilizing group, and

(4) neutralizing the stabilizing group-oligopeptide-therapeutic agent with a pharmaceutically acceptable salt.

108. The method of claim 107, wherein the trityl-protected oligopeptide is the trityl-protected β-AlaLeuAlaLeu.

109. The method of claim 107, wherein the therapeutic agent is an anthracycline.

110. The method of claim 107, wherein the step of activating the trityl-protected oligopeptide with an activating agent further comprises selecting an active agent from the group consisting of HATU, HBTU, DCC, DIC, DCC+HOBt, EDC, OSu, and PyBOP.

111. The method of claim 107, wherein the step of reacting the oligopeptide therapeutic agent with a stabilizing group further comprises use of an anhydride or an activated ester of the stabilizing group.

112. The method of claim 111, wherein the step of reacting the oligopeptide therapeutic agent with a stabilizing group further comprises using a succinic or glutaric anhydride or respective methyl hemiester of succinic acid or glutaric acid as the stabilizing group.

113. The method of claim 107, wherein the step of neutralizing the stabilizing group-oligopeptide-therapeutic agent further comprises using a sodium bicarbonate conjugate as the pharmaceutically acceptable salt.

114. The method of claim 107, wherein the concentration of trityl-protected oligopeptide therapeutic agent conjugate in the activating step is 1-25 %.

115. A composition made by the method of claim 107.

116. A compound selected from the group consisting of: Suc-βAla-Leu-Ala-Leu-Dox, Suc-βAla-Leu-Ala-Leu-Dnr, and Glutaryl-βAla-Leu-Ala-Leu-Dox.

117. A compound selected from the group consisting of:

βAla -Leu-Ala-Leu-Dox

Trityl-βAla -Leu-Ala-Leu-Dox

Diphenylmethyl-βAla -Leu-Ala-Leu-Dox

Benzyloxycarbonyl-βAla -Leu-Ala-Leu-Dox

Fmoc-βAla -Leu-Ala-Leu-OBn

βAla -Leu-Ala-Leu-OBn

Methyl-succinyl-βAla -Leu-Ala-Leu-OBn

Methyl-succinyl-βAla -Leu-Ala-Leu

Fmoc-βAla -Leu-Ala-Leu

Fmoc-Thi-Tyr-Gly-Leu

Fmoc-βAla -Leu-Ala-Leu-Dnr

Fmoc-Thi-Tyr-Gly-Leu-Dnr

Suc-Thi-Tyr-Gly-Leu-Dnr

Gl-βAla -Leu-Ala-Leu-Dox

βAla -Leu-Ala-Leu-Dox Lactate

Allyl-succinyl-βAla -Leu-Ala-Leu-Dox

Suc-βAla -Leu-Ala-Leu

Methyl esters of Suc-βAla -Leu-Ala-Leu

Fmoc-βAla -Leu-Ala-Leu-Dox

Methyl-succinyl-βAla -Leu-Ala-Leu-Dox, and

Allyl-hemi succinate.